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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/812,308	03/30/2004	Luca Battistini	GRT/4865-38	1799

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EXAMINER	
RAE, CHARLESWORTH E	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/812,308	BATTISTINI ET AL.	
	Examiner	Art Unit	
	Charleswort Rae	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 3/28/07, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Summary of applicant's arguments

Claim of Priority

Applicant contends that the request for claim of priority of the instant application from application No. 10/137,699 (appl. '699), which is the parent of the Int'l Application No. PCT/IT03/00237 from which the instant application claims benefit, should be granted as appl. '699 provides detailed and complete support for autoimmune diseases (see page 3 of applicant's Response received 3/28/07; see also page 4 of applicant's Response received 7/17/06). Applicant contends that to the extent that appl. '699 discloses some specific examples of autoimmune diseases; namely, multiple sclerosis, systemic lupus erythematosus, and rheumatoid arthritis, there is no need to provide literal support in a parent application for a subsequent example of carrying out the invention that is claimed in a child application. Although uveitis is not disclosed in appl.

'699, applicant further contends that the general concept of "autoimmune disease" as embodied in appl. '699 provides the necessary support for uveitis as claimed in the instant application. Therefore, applicant's claim of priority benefit of appln. '699 is proper.

As previously made of record, for example, in Office action mailed 11/29/06, applicant's argument is not deemed persuasive as the claims of the instant application are directed toward subject matter which was not disclosed in appl. '699; namely, uveitis. **As applicant states on the last paragraph on page 4 of applicant's Response received 3/28/07, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, and uveitis all belong to the genus of autoimmune diseases, but each one is a different disease.** Further, in the absence of the specific uveitis disclosure provided by Int'l Application No. PCT/IT03/00237 from which the instant application claims benefit, the instant application would reasonably lack the necessary support for the uveitis subject matter. Thus, the prior decision denying the grant of claim of priority from parent appl. '699 with respect to the uveitis subject matter is maintained.

Claim rejections under 35 USC 112, second paragraph

Applicant amendment of claim 9, deleting the term "effective amount," overcomes the rejection. Thus, this rejection is withdrawn.

Claim rejections under 35 USC 102

On pages 4-5 of applicant's Response of 3/28/07, applicant contends that the rejected claims are not anticipated by the cited reference (Mistrello et al., US Patent 6,797,722) because the cited reference does not teach uveitis. Applicant further states that "one species of the genus cannot anticipate a different species of the same genus as anticipation requires each and every limitation to be taught in the reference."

Applicant's argument is not deemed persuasive for the reasons already made of record, for example, in the Office action mailed 11/29/06 (pages 3-4), and for the reasons stated herein.

To reiterate, Mistrello et al. teach the administration of effective amounts (2 mg/kg/day) of the identical drug (i.e. DLTIII-IT) as claimed in the instant application, to female rats with polyarthritis; Mistrello also teach that the drug is an effective immunosuppressant. Msitrello et al. also disclose that DLTIII-IT may be useful as a therapeutic agent in clinical medicine (pages 163-168). The only method step recited in the instant claims is the step of administering the said identical drug taught by Mistrello et al. To the extent that Mistrello et al. teach the same method step as claimed in the instant application, coupled with the fact that polyarthritis and uveitis are both autoimmune diseases, and the effect to be achieved in treating uveitis and polyarthritis with the claimed active agent is the same i.e. immunosuppression, it necessarily follows that the immunosuppressive action to be achieved in administering the claimed drug is an inherent property. Also, the uveitis and polyarthritis treatment groups overlap as

evidenced by the teaching of Kawahito et al. (Kawahito et al. Localization of quantitative trait loci regulating adjuvantinduced arthritis in rats: evidence of genetic factors common to multiple autoimmune diseases. The Journal of Immmunology. 1998; 161:4411-4419, electronic pages 1-19).

Mistreollo disclose that DL111-IT when given to rats at the dose of 2 mg/kg/day, the drug did not exhibit any anti-inflammatory activity (page 167, column 1, second paragraph, first line to page 8, first column, line 2); however, the ant-inflammatory activity of the drug was not evaluated at higher doses. This lack of anti-inflammatory activity of DLTIII-IT at this dosage level bolsters the argument that the primary action of DLTIII-IT is immunosuppression, rather than anti-inflammatory, such that someone of skill in the art would reasonably envision that the administration of an identical dose of DLTIII-IT to subjects suffering from uveitis and polyarthritis would necessarily effectuate an immunosuppressive effect in treating both uveitis and polyarthritis due to a shared underlying automimmune process as evidenced by Kawahito et al. (Kawahito et al. Localization of quantitative trait loci regulating adjuvant induced arthritis in rats: evidence of genetic factors common to multiple autoimmune diseases. The Journal of Immmunology. 1998; 161:4411-4419, electronic pages 1-19).

Kawahito et al. teach that rat models appear to provide a powerful complementary approach to identify and characterize candidate genes that may contribute to autoimmune diseases in several species (abstract). Kawahito et al. teach that adjuvant-induced arthritis (AIA) in rats is a widely used autoimmune experimental model with many features similar to rheumatoid arthritis (RA) (abstract). Kawahito et al.

also disclose study data of collagen-induced arthritis (CIA). Kawahito et al. teach that AIA predominantly involves T cell-mediated mechanisms, whereas CIA requires both humoral and cellular immunity (page 2, last paragraph, last line to page 3, line 1) Kawahito et al teach that the quantitative trait loci (QTL) region on chromosome 4 (*Aia3/Cia3*), like the MHC, appears to be involved in several other autoimmune diseases in rats, including insulin-dependent diabetes, thyroiditis, and experimental autoimmune uveitis (abstract). Kowahito et al. teach that an analysis of conserved synteny among rats, mice, and humans suggested that Aia2 and *Aia3/cia3*, like *Aia1/Cia1*, contain candidate genes for several autoimmune/inflammatory diseases in mice and humans, including diabetes, systemic lupus erythematosus, inflammatory bowel disease, asthma/atopy, multiple sclerosis, and RA (abstract).

For these reasons stated above and the reasons already made of record, this rejection is maintained as applicant's argument is not found to be persuasive and the claim amendments fail to overcome the rejection.

Claim rejections under 103(a)

Applicant contends the following:

1) The claim rejection should be withdrawn because the invention as claimed would not have been obvious to one of ordinary skill in the art at the time it was made.

2) Based on the teaching of Mistrello et al. that: a) DLTIII-IT was unsuccessful in treating arthritis i.e. clearly ineffective in treating arthritis, b)

DLTIII-IT possesses immunosuppressive activity, and c) DLTIII-IT is useful in the treatment of heterologous skin transplantation (see applicant's Response of 3/28/07, page 5, last paragraph), and d) the use of ST1959 as disclosed by the reference is not sufficient to establish that it is effective in treating any autoimmune disease, especially uveitis, there is no reasonable expectation of success.

3) Mozes et al. does not remedy the deficiency of Mistrello et al.

4) Prima facie case of obviousness is not established as all the claim limitations are not taught by the prior art in accordance with MPEP 2143.03.

Applicant's arguments have been considered but are not deemed to be persuasive for the reasons already made of record, for example, in the Office action mailed 11/29/06, and for the reasons stated herein.

It is noted that applicant's proffered arguments essentially assert that someone of skill in the art at the time invention was made would not have reasonably expected that administering the dose of DLTIII-IT taught by Mistrello et al. would exhibit immunosuppressive effects in treating subjects suffering from uveitis.

It is further noted that applicant's argument regarding the lack of anti-RA activity of DLTIII-IT disclosed by Mistrello et al. as evidence of an attendant lack of immunosuppressive activity is erroneous. Mistreollo disclose that DL111-IT when given to rats at the dose of 2 mg/kg/day, the drug did not exhibit any anti-inflammatory activity (page 167, column 1, second paragraph, first line to page 8, first column, line 2); however, the ant-inflammatory activity of the drug was not evaluated at higher doses.

This lack of anti-inflammatory activity of DLTIII-IT at this dosage level bolsters the argument that the primary action of DLTIII-IT is immunosuppression, rather than anti-inflammatory, such that someone of skill in the art would reasonably envision that the administration of an identical dose of DLTIII-IT to subjects suffering from uveitis and polyarthritis would necessarily effectuate an immunosuppressive effect in treating both uveitis and polyarthritis due to a shared underlying automimmune process in view of Mistrollo et al., and further in view of Mozes et al.

The discussion of Mozes et al. made of record in the Office action mailed 11/29/06 is incorporated by reference (see page 5, last two paragraphs). To reiterate, Mozes et al. teach, for example, DBA mouse strains models for inducing experimental SLE autoimmune disease, while Mistrello et al. teach DBA experimental rat models for evaluating the immunosuppressive effects of DLIII-IT. To the extent that Mozes et al. teach SLE autoimmune rat models, someone of skill in the art at the time the instant invention was made would have been motivated to combine the teaching of Mistrello et al. and Mozes et al. to create the instant inventive concept of a method for treating autoimmune diseases, including SLE autoimmune disease and uveitis, with DLTIII-IT, as evidenced by the above discussion of Kawahito et al. in connection with the claim rejection under 102(b) (Kawahito et al. Localization of quantitative trait loci regulating adjuvant induced arthritis in rats: evidence of genetic factors common to multiple autoimmune diseases. The Journal of Immmunology. 1998; 161:4411-4419, electronic pages 1-19).

Further, based on the teaching of Mistrello et al., it would have been routine for someone of skill in the art at the time the instant invention was made to would administer different doses of DLTIII-IT to illicit an immunosuppressive effect in a mammal as instant claim 11 does not set forth a limit on the actual dose of DLTIII-IT that is required to be administered to treat uveitis.

Based on the suggestion of Mistrello et al. that DLTIII-IT would be useful as a therapeutic agent in clinical medicine (pages 163-168), someone of skill in the art at the time the instant invention was made would have found it obvious to create the instant claimed invention with a reasonable expectation of success, absent any evidence to the contrary.

Thus, this rejection is maintained for the above reasons.

Claim rejections – 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-10 are rejected under 35 USC 102(b) as being anticipated by Mistrello et al. (already made of record).

The above response to applicant's arguments is incorporated by reference.

For the reasons stated above in response to applicant's arguments, claims 9-10 are rejected as being anticipated by Mistrello et al. as the instant claims recite the administering of DLTIII-IT as the only active method step which is identical to the teaching of Mistrello et al. of administering DLTIII-IT to a mouse with polyarthritis. instant claims 9-10 are anticipated by Mistrello et al. as someone of skill in the art would reasonably envision that administering DLTIII-IT in immunosuppressive doses would necessarily effectuate immunosuppression in uveitis and polyarthritis treatment populations as evidenced by a shared immunological mechanism among certain autoimmune diseases, including arthritis and immune uveitis, taught by Kowahito et al., as the immunosuppressive activity of DLTIII-IT is an inherent characteristic of DLTIII-IT (which is distinct from any anti-inflammatory activity). Applicant is invited to provide evidence to contrary, however.

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mistrello et al., supra, in further view of Mozes et al. (Genetic Analysis of Experimentally Induced Lupus in Mice, Clinical Immunology and Immunopathology, 1997, 85(1):28-34).

The above discussion in response to applicant's arguments in connection with the rejection under 103(a) is incorporated by reference.

To reiterate, Mistrello et al. and Mozes et al. do not teach uveitis.

Claim 11 is directed to human. Mistrello et al. teach mammal. Based on the desirable therapeutic benefits achieved in the female mice with polyarthritis and the expressed need for more selective and less toxic immunosppressants, coupled with the teaching that at least suggest suggest that DL111-IT would be useful as a therapeutic agent in clinical medicine (see Mistrello et al, pages 163 and168), someone of skill in the art at the time the instant invention was created would have been motivated to combine the teaching of Mistrello et al., in view of Mozes et al. to create the instant inventive concept.

Thus, someone of skill in the art would have found it obvious to combine the teaching of Mistrello et al., in view of Mozes et al., to create the instant claimed invention with a reasonable expectation of success that DL111-IT would exhibit immunosuppressive activity in humans suffering from uveitis as evidenced by evidenced

by the above discussion of Kawahito et al. in connection with the claim rejection under 102(b) (Kawahito et al. Localization of quantitative trait loci regulating adjuvant induced arthritis in rats: evidence of genetic factors common to multiple autoimmune diseases. The Journal of Immmunology. 1998; 161:4411-4419, electronic pages 1-19).

New Rejection under 112, 1st paragraph – New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF WRITTEN DESCRIPTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

Claims 9-11 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant invention is directed towards a method for treating uveitis in a subject in need thereof, comprising administering 3-(2-ethylphenyl)-5-(3-methoxyphenyl)-1H1,2,4,-triazole to said subject. Clearly, the instant application disclosure discloses that it is an object of the present invention a method for treating a subject affected by an autoimmune disease comprising administering to said subject an effective amount of (3-(2-ethylphenyl)-5-methoxyphenyl)-1H-[1,2,4]-triazole (Instant US Patent Application Publication No.

20050026980, paragraph 0013). The scope of the instant claims have been broadened by amendment of the instant claims by requiring any amount of (3-(2-ethylphenyl)-5-methoxyphenyl)-1H-[1,2,4]-triazole to be administered for treating uveitis in a subject in need thereof. This is a new matter rejection.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 8 a.m. to 4:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

31 May 2007
CER

BRIAN-YONG S. KWON
PRIMARY EXAMINER